Modeling the Chikungunya Virus: A System Dynamics Approach

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Abstract

The Chikungunya virus (CHIKV) is a mosquito-borne viral infection of humans that, although rarely fatal, can cause fever, severe joint pain, muscle pain, headache, nausea, fatigue, and occasionally a rash. System dynamics modeling is a highly applicable approach that develops a perspective and a set of conceptual tools to understand the structure and dynamics of complex systems such as the spread of CHIKV. Using a rigorous, iterative modeling method, both structure and dynamics are translated into a formal computer simulation that models the complex behavior of the system. This simulation captures the system's key variables and their interactions and allows for the design and evaluation of policies associated with combatting the spread of CHIKV. In order to most accurately model the spread of CHIKV, a variety of applicable real world data is initially analyzed and calibrated to determine key model parameters and variable relationships. These parameters and relationships are then formally incorporated into the system dynamics model and can be continually refined as new data or additional information is learned about the spread of CHIKV.

Key Words: Infectious Disease, System Dynamics, Chikungunya Virus

Introduction

Chikungunya (CHIKV) recently emerged in the Caribbean when the first cases were reported from St. Martin in early December, 2013. The virus quickly spread throughout the Eastern Caribbean islands from April to May of 2014 and reached Florida in July of 2014 (European Centre for Disease Prevention and Control, 2014). As of January 30, 2015, the Pan American Health Organization reported 24,521 confirmed and 1,155,354 suspected CHIKV cases in the Americas (Pan American Health Organization, 2015). The CHIKV virus causes fever, severe joint and muscle pain, headache, nausea, fatigue, and occasionally a rash during the acute infection period and severe joint pain may persist for well after the infection (Center for Disease Control, 2011). The virus is rarely fatal; however, it may prove fatal in patients with additional health concerns. While there is some treatment for the individual symptoms, there is no specific treatment for the disease.

The interactions between humans and the mosquito population drive the dynamics of the spread of CHIKV. Nasci summarized the key variables to capture in modeling the spread of CHIKV as the following: type of mosquito (*aedes aegypti and aedes albopictus*), western hemisphere human movement patterns, CHIKV genotypes and mutations or in other words the virus lineage (East-Central-South African (ECSA), West African, and Asian); personal protection measures, vector control efforts and preparedness and response plans (Nasci, 2014). More specifically, these variables must capture the dynamics of the mosquito population, the dynamics of the host or human population, the transmission dynamics between the human and mosquito populations, the vector control efforts that influence the mosquito population dynamics, and the personal protective measures that influence the host population dynamics.

System Dynamics provides an approach to model and understand the dynamic complexity that exists within systems, allows the ability to simulate the behavior of systems over time, can help adjust individuals' mental models of the system, and can lead to implementation of policies to improve system behavior. System Dynamics attempts to understand the dynamic complexity that is inherent in any natural or human system. Dynamics are the behavior of a system over time, which are generally complex and non-linear in nature (Forrester, 1961). Even the simplest of systems, with apparently low levels of structural complexity, can exhibit high levels of dynamic complexity. This complexity comes from feedback within the system, time delays between decisions and effects, and the learning process of the system (Sterman, 2000). Applications of System Dynamics have provided insights into the dynamics of several different areas including corporate policy, the dynamics of infectious disease and diabetes, drug addiction in a community, and the dynamics of commodity markets (Forrester, 1971). This paper relies heavily on System Dynamics to better understand the spread of the CHIKV virus and develop potential policies for mitigating the spread of the epidemic.

Literature Review

Much of the literature in modeling mosquito-borne pathogens references the Ross-McDonald Theory, which was firmly established in 1970 (Reiner, et al., 2013). Reiner et. al. reviewed 388 models and found most closely resemble the Ross-McDonald theory. The authors identified the need to expand the theory "around the concepts of heterogeneous mosquito biting, poorly mixed-host encounters, spatial heterogeneity, and temporal variation in the transmission process" (Reiner, et al., 2013). The questionnaire used to evaluate the models provides an initial guide in identifying key variables among the three common components that are essential to these models: a host, a mosquito, and encounters between the two. Many aspects of the varying models referenced by the author could potentially serve to inform parameters or variables within a system dynamics model.

Several sources were essential to understanding the key variables that were required to model the spread of an infectious disease. Smith, et Al. summarizes the Ross-McDonald Theory, clearly defining the model's notation and providing an initial starting point in identifying the key parameters and variables for a system dynamics model. Additionally, the summary discusses several dynamic relationships that are essential to modeling the CHIKV epidemic (Smith, et al., 2012). In his work, Nasci identifies potential state variables and some limited associated source data and identifies the similarity of CHIKV transmission ecology to the dengue virus. Key variables and dynamics to consider include: 1) type of mosquito (*aedes aegypti and aedes albopictus*), 2) western hemisphere human movement patterns, 3) CHIKV genotypes and mutations or in other words the virus lineage (East-Central-South African (ECSA), West African, and Asian), 4) personal protection measures, 5) vector control efforts and 6) preparedness and response plans. Additionally, he describes the potential to use historical dengue virus transmission and control efforts that exists for model calibration in the absence of data on CHIKV (Nasci, 2014).

Another key aspect of modeling the spread of CHIKV is understanding the human travel patterns that spread the virus. With the short lifespan and travel distance of mosquitoes, it is highly unlikely that they are responsible for the virus moving through the Caribbean. Khan, et al. analyzes air travel in comparison to mosquito distribution (*aedes aegypti and aedes albopictus*) in the western hemisphere to identify potential spread of CHIKV (2014). Temporal and spatial dynamics of travel and global warming leads to increased potential mosquito habitats are addressed. As a potential policy consideration, the authors also address some temporal prevention when host viremia is the greatest (Khan, et al., 2014). Cauchemez et al. attempt to characterize CHIKV transmission in terms of population movements with the goal to inform resource allocation for monitoring and controlling through their data analysis of CHIKV spread on three islands in the Caribbean. The resulting analysis suggests the growth is exponential. Additionally, Cauchemez et al., attempt to inform spread through regional movement dynamics, identifying "most probable" source of transmission for areas (2014).

As a comparison, in the article investigating the spread of influenza Shaman, et al. developed a forecast of the intensity and timing of influenza to improve focus on mitigation and response resources. Their analysis, based on a simple SIRS (susceptible-infected-recovered-susceptible) model, highlights aspects of the SIRS model that are applicable to the CHIKV system dynamics development and highlights potential mitigation approaches (Shaman, Karspeck, Yang, Tamerius, & Lipsitch, 2013).

The distribution of potentially infectious mosquitoes is important to consider in mosquito population and transmission dynamics. Foley, et al. developed a web application that provides a spatial database of mosquito species with vector borne diseases. The database could potentially provide spatial distribution throughout the Western Hemisphere of the aedes aegypti and aedes albopictus mosquito types that spread CHIKV (Foley, et al., 2010). Volk et al. also consider the genomic differences in varying strains of CHIKV to inform different epidemic transmission patterns. The authors suggest that due to similarities between dengue and CHIKV, CHIKV is likely grossly underreported. Their analysis identified the three geographically associated genotypes (West African, East-Central-South African (ECSA) and Asian) and they investigated numerous strains derived from these genotypes (Volk, et al., 2010). Staples, et al. identified several factors that contribute to CHIKV spread such as "high attack rates associated with recurring epidemics, high levels of viremia associated with infection in humans, and the worldwide distribution of vectors responsible for transmitting CHIKV" (2009). They recommended priorities for additional studies to include evaluating vector competence and potential transmission factors to provide insight into the effectiveness of strains; and development of models incorporating ecologic, entomologic, and virologic factors that contribute to the spread of CHIKV (Staples, Breiman, & Powers, 2009).

Several sources emphasize the potential policies to consider in combatting the spread of CHIKV. Gibney, et al., described the epidemiology of confirmed CHIKV cases in the U.S. and compared them with returning viremic CHIKV cases, thereby identifying potential risk measures of transmission (2011). The article highlights the importance of recognition, diagnosis, and reporting of CHIKV. This article provides some useful data analysis based on available infection data in the U.S. and highlights "ArboNET" as the database utilized to track CHIKV epidemiology. (Gibney, et al., 2011). "ArboNET is a national arboviral surveillance system managed by CDC and state health departments. In addition to human disease, ArboNET maintains data on arboviral infections among presumptive viremic blood donors, veterinary disease cases, mosquitoes, dead birds, and sentinel animals" (Centers for Disease Control and Prevention, 2014). The Center for Disease Control and Prevention also provides a robust website specific to CHIKV prevention with many useful links to additional sources (2014). The

European Centre for Disease Prevention and Control also provides a useful summary focused on mitigation policies. They provide a "Rapid Risk Assessment: Chikungunya Outbreak in Carribean Region (25 June 2014)." Consistent with the other literature, their risk assessment summarizes several key points to prevent the spread of CHIKV. Potential policies include reducing exposure to aedes aegypti and aedes albopictus mosquitos, preventing exposure through personal protection against mosquito bites, conducting and vector control, and seeking medical care if presenting with CHIKV after returning from an exposed area. Additional preparedness efforts should also be considered, such as strengthened surveillance systems, rapid notification of cases, review of contingency plans for mosquito-borne outbreaks, education and collaboration of the general public in the control of mosquito breeding sites, strengthened vector surveillance systems and rapid implementation of vector control measures around each case (European Centre for Disease Prevention and Control, 2014).

System Structure

Epidemics of infections typically follow an S-shaped growth pattern. The cumulative number of cases will grow initially slowly until hitting a critical mass of infections that begin to spread exponentially. The epidemic then begins to taper as the epidemic ends and/or health organizations take action to mitigate the epidemic. This Susceptible, Infected, Recovered (SIR) model captures this model very well as demonstrated by the basic model of the SARS epidemic in Taiwan (Repenning, 2013). Figure 1 presents the basic stock and flow diagram for a SIR Model. One of the interesting aspects of the structure for the CHIKV epidemic is that there are two populations that must interact for the virus to spread.

Figure 1: Basic SIR Model Structure

Interactions of several subsystems drive the dynamics and spread of CHIKV in the Western Hemisphere. First, the mosquito population system determines the number of susceptible mosquitoes in an area. Second, a human population system that accounts for the human dynamics in the area. However, neither group can spread the CHIKV on their own as transmission of the disease only happens between a viremic human and a susceptible mosquito or between an infected mosquito and a susceptible human. This cycle reinforces itself with more and more mosquitoes infecting more and more humans and vice versa. CHIKV spread quickly becomes exponential unless health officials bring to bear external policies to the problem. Our system structure first looks at the mosquito population and the human population and then incorporates the two.

Mosquito Population: The mosquito population is initialized with an initial stock of "Mosquito Eggs" and an "Initial Mosquito Population." Figure 2 presents the causal loop diagram for the mosquito population to visualize the dynamics of the mosquito population without the virus. If left to its own accord in ideal conditions, the mosquito population would continue to lay eggs, eggs would continue to hatch, and the mosquito population would continue to grow with no infected mosquitoes. Eggs and mosquitoes would die off based on their typical lifecycle attributes. As a consideration, climate clearly has an impact on mosquito viability, and only two types of mosquito species are considered, as aedes aegypti and aedes albopictus are the two species that can transmit CHIKV.

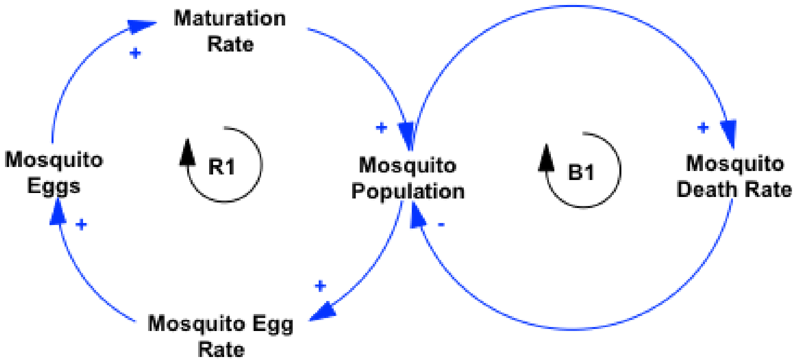


Figure 2: Mosquito Population Causal Loop Diagram

Human Population: In the human population model, a country's population represents the initial "Susceptible Human Population." The "Infected Human Population" becomes initialized in time (minimum infected is 1) based on when the Pan American Health Organization (PAHO) first reported a case of CHIKV in the country. This reported infection (or infections) initializes the transmission dynamics between the mosquito and the human populations. On average the CHIKV virus will incubate in the "Infected Human Population" for 5 days before the human enters the stock of "Viremic Human Population." A human is viremic on average 7-days before entering the stock of "Recovered Human Population" where the human is now considered immune. Transmission dynamics from human to mosquito occur only when the human is viremic.

Human / Mosquito Infection Transmission Dynamics: The transmission dynamics between populations begin when a mosquito from the stock of "Susceptible Mosquito Population" bites a viremic human. The mosquito enters the "Infected Mosquito Population" where the virus incubates on average 7 days. The mosquito then flows into the "Infective Mosquito Population" and is now a threat to infect humans with the virus. Now viremic mosquitoes begin interacting with the "Susceptible Human Population" creating an increase in the "Infected Human Population". The cycle now can repeat itself as viremic mosquitoes infect humans and viremic humans continue to infect mosquitoes. This reinforcing loop if left unabated will continue to increase and grow exponentially. Figure 3 presents the overall causal loop diagram that depicts the interaction between the human and mosquito population that results in the transmission of the virus.

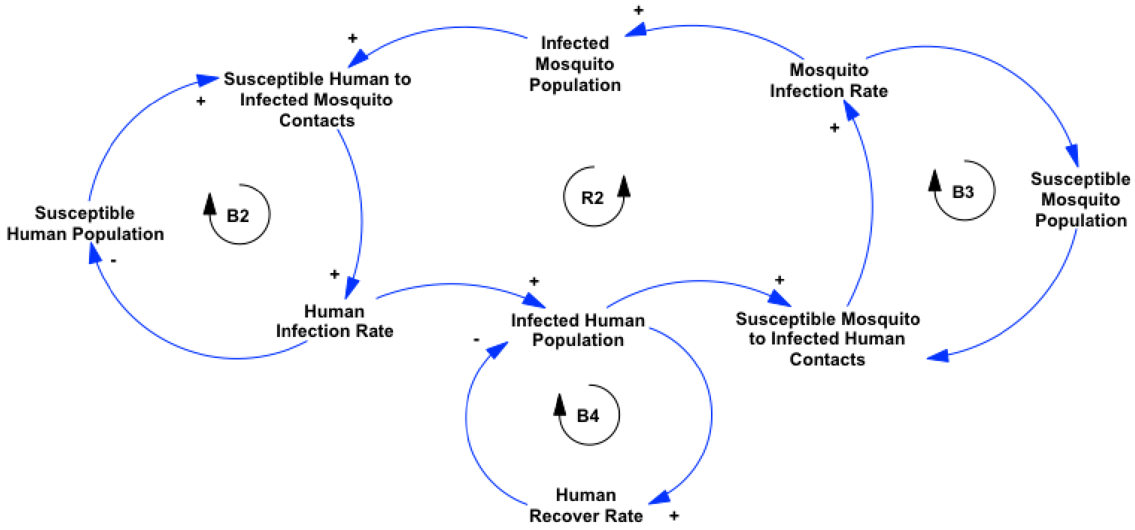


Figure 3: Interaction Causal Loop Diagram

System Dynamics Model

System Dynamics models build upon the causal loop diagrams used to understand the structure of the system and introduce stocks and flows. A stock is a measurable accumulation of material in a system. A flow is an instantaneous rate of change of material between stocks in a model (Forrester, 1961). Mathematically, the value of the stock is equal to the integral of the combined inflows and outflows into and out of the stock. Stocks and flows enable the model to account for delays inherent to the system, such as the incubation period or the time period a mosquito or human is contagious. The model uses this basic structure to capture the interactions of the mosquito and human population to model and simulate the dynamic behavior of the CHIKV epidemic.

In developing an understanding of the system and its interactions and feedback structure, we expand on the basic premise that the spread of CHIKV requires a mosquito, a host, and an interaction between the two. We initially model two different subsystems—creating a mosquito population model and a human population model—and then link the two models together through the interactions that occur between the two populations. Since conditions in each country differ, the model adapts to each individual country using different initial conditions to model the spread of CHIKV.

Figure 4 presents the mosquito sub-system model, which is a series of stocks and flows that takes the mosquito population from the egg to the susceptible population. From the susceptible population, interactions with the human population cause a portion of the adult mosquito population to become infected. Although there are several stages in the mosquito's maturation from egg to larva to adult, the model does not account for these stages, as they are not critical to understanding the transmission of CHIKV (Singapore National Environment Agency, 2013). The model does account for the *Average Incubation Period* of the virus, which is 7 days, during which the mosquito is infected, but cannot spread the disease to humans (Center for Disease Control, 2011). The model also accounts for various vector control policies by incorporating them into the mosquito death rates along with the normal mosquito death rate due to their 14-day life span (Singapore National Environment Agency, 2013). The initial model was set to equilibrium by adjusting the effects of vector control on the death rate to ensure that the mosquito population did not experience exponential growth.

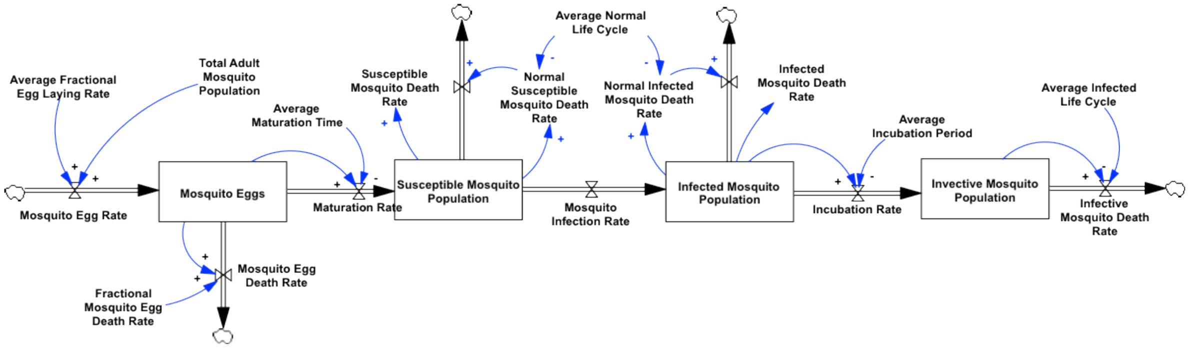


Figure 4: Mosquito Population Sub-System Model

Figure 5 presents the human population sub-system model. Due to the short duration of the CHIKV epidemic, the model does not need to simulate the entire human lifecycle; thus we can assume that population size remains relatively fixed over the duration of the epidemic. This model only accounts for the *Susceptible Human Population*, the *Infected Human Population*, the *Viremic Population* and the *Recovered Human Population*. Unlike mosquitoes, humans can transmit the virus to mosquitoes during the viremic or infected phase of the virus (Center for Disease Control, 2011). The variables for *Average Human Incubation Period* (5 days), and *Average Time to Recovery* (7 days) are all based on studies by the CDC (Center for Disease Control, 2011). It is important to make these two populations distinct because only the viremic population would show signs of the virus and seek medical attention, but there would still be the possibility to transmit the disease to mosquitoes without the human knowing they had CHIKV.

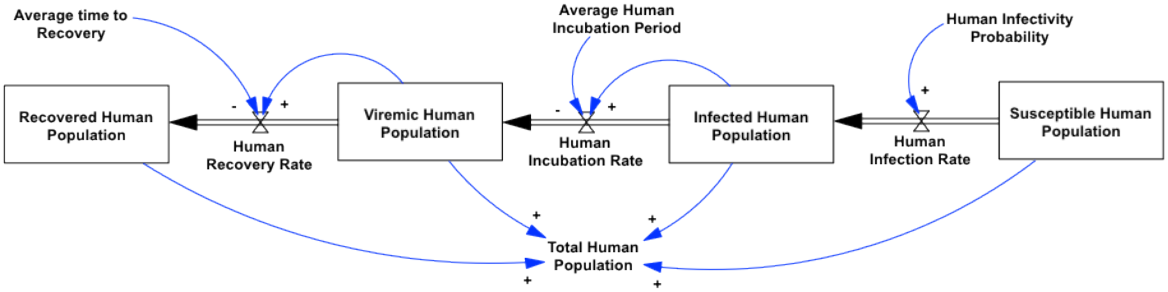


Figure 5: Human Population Sub-System Model

Figure 6 presents the portion of the model that captures the dynamics of the transfer of the virus between the mosquito and human populations. It is similar to the basic SIR model, however, instead of an interaction between individuals in the same population, the CHIKV virus requires the interaction of an infected mosquito or human with a susceptible member of the other population. Two key variables that affect the transmission of the disease between humans and mosquitoes are the *Mosquito Infectivity Probability* (0.75) and the *Human Infectivity Probability* (0.80) that determine what contacts result in transmission of the disease (Poletti, et al., 2011). There is accurate data on the number of feedings per day as well as the mosquito infectivity probability; however, data for average mosquito contacts per person is not readily available. So, this variable becomes essential to calibrate the model to simulate actual data.

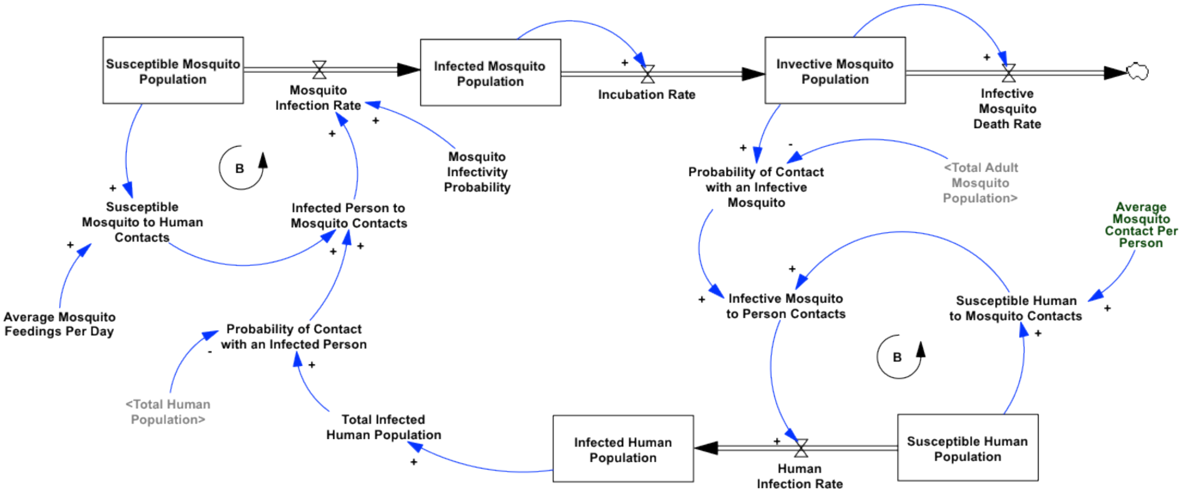


Figure 6: CHIKV Transmission Model

In addition to the transmission dynamics between the two populations, the model attempts to replicate historic data by capturing the *Cumulative Reported Cases* of CHIKV. The stock of cumulative reported cases utilizes the *Human Infection Rate* and the *Probability of Reporting* to model the number of cases. The variable *Probability of Reporting* captures several aspects of the virus as a constant in the model. First, the symptoms of CHIKV may be similar to other common illnesses, so people may not go to a hospital or clinic for treatment. Volk et al. note this as a major problem in tracking the CHIKV virus because of its similarities to the dengue virus (2010). Second, depending on the country's medical infrastructure, cases may go unreported. Although historic data exists for nearly every country in which the CHIKV virus exists, this paper focuses on simulating the behavior in St. Martin and Martinique, two of the first countries to report the epidemic in the Caribbean.

Model Output and Validation

The model generates the S-shaped growth that one would expect of an epidemic such as CHIKV and follows the same pattern as the historic data from St. Martin and Martinique. However, the magnitude of the spread of the disease and the timing of the S-shaped growth did not match historic data given the model's initial assumptions about the calibration variables. The calibration variables are the *Average Mosquito Contacts per Person* and the *Probability of Reporting*. *Probability of Reporting* accounts for the probability of a person reporting the illness and takes into account several factors, including the fact that only a certain percent will actually develop symptoms despite being infected. In addition, this variable could vary by country based on access to healthcare facilities and cultural differences. The *Average Mosquito Contact per Person* is the average number of mosquito to human contacts per day. Again, this variable enables the calibration of the model as different countries could have differing conditions that lead to human exposure to mosquitoes.

	Total Population	Initial Infected	Week 32 Infected		Probability of Reporting	Avg Mosquito Contact Per Person	R^2
			Actual	Model			
St. Martin	74852	89	4653	5243	0.075	0.75	0.67
Martinique	386486	8	57435	66152	0.22	0.6	0.61

Table 1: Model Summary Table for Key Variables

Table 1 presents a summary of the key variables for both St. Martin and Martinique for the CHIKV epidemic. In both cases, the model predicted slightly more cases than were actually reported. The PAHO tracks the spread of the CHIKV epidemic to include the data for the total population, initial number of reported infections, and number of reported cases for Week 32 (2015). The coefficient of correlation was relatively high for the simulation; however, more refinement of the model could be performed to increase these values. However, the model does generate similar behavior to the historic data and the magnitude and shape of the curves are consistent.

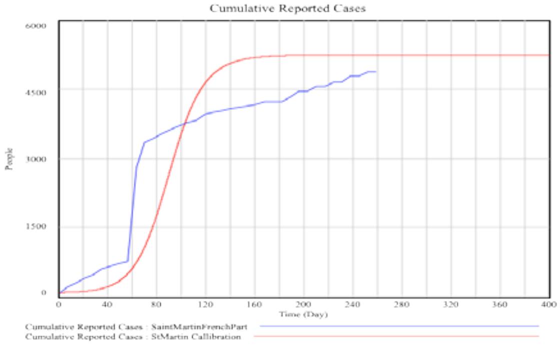


Figure 7: St. Martin CHIKV Reported Cases

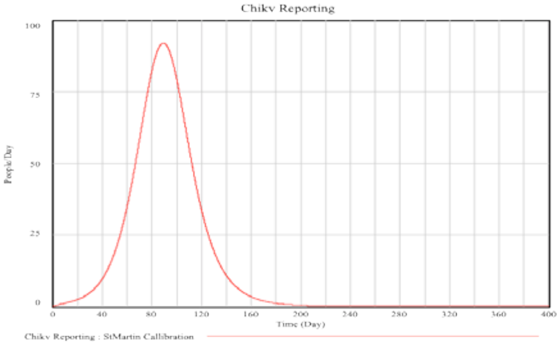


Figure 8: St. Martin CHIKV Reporting

The historic data from St. Martin in Figure 7 is consistent with the S-shaped growth hypothesized for an epidemic such as CHIKV. Also depicted by Figure 7, the model simulates behavior very similar to the historic data in St. Martin. Although historic data of the CHIKV reporting is not available, an important aspect to modeling the spread of CHIKV is the rate at which people report the virus as depicted in Figure 8.

Week	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32
Actual	89	294	477	601	711	2795	3422	3630	3773	3953	4033	4113	4173	4223	4333	4453	4553
Model	89	100	136	173	333	725	1541	2758	3908	4621	4967	5122	5190	5220	5234	5240	5242
Delta	0	-194	-341	-428	-378	-2070	-1881	-872	135	668	934	1009	1017	997	901	787	689

Table 2: Model Data Comparison for St. Martin through Week 32

Table 2 presents a bi-weekly summary of the actual reported cases of CHIKV and the output of the model along with a delta between the two. For St. Martin, the actual reported cases experience rapid growth between weeks 8 and 10 that the model was unable to simulate effectively. For the first 14 weeks, the output of the model lags behind the actual data. However, after week 16, the output of the model is slightly higher than the actual reported cases. The two sets of data are somewhat correlated with each other as the coefficient of correlation is 0.67, which is not great, but does indicate some level of correlation. The model does generate similar behavior to the actual spread of the CHIKV virus and can provide valuable insights for potential policy alternatives to avert the epidemic earlier in time horizon.

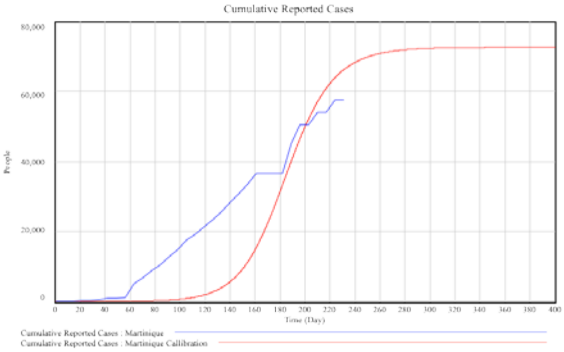


Figure 9: Martinique CHIKV Reported Cases

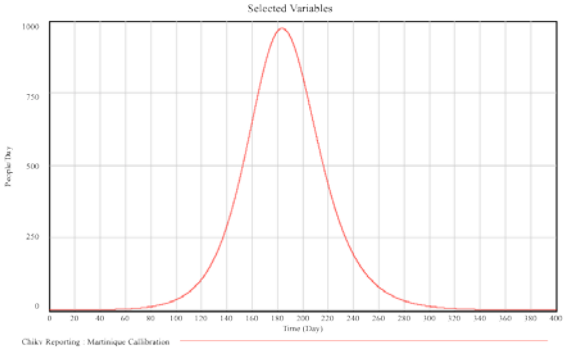


Figure 10: Martinique CHIKV Reporting

Like St. Martin, the historic data for Martinique, in Figure 9, follows the S-shaped growth pattern; however, it does not experience the exponential growth like St. Martin did around week 10. Figure 9 also present the simulated behavior from the model, which generates similar behavior over time. Figure 10 presents the output of the rate of reporting the CHIKV virus from the simulation, which has a similar pattern to St. Martin but occurs later in the simulation.

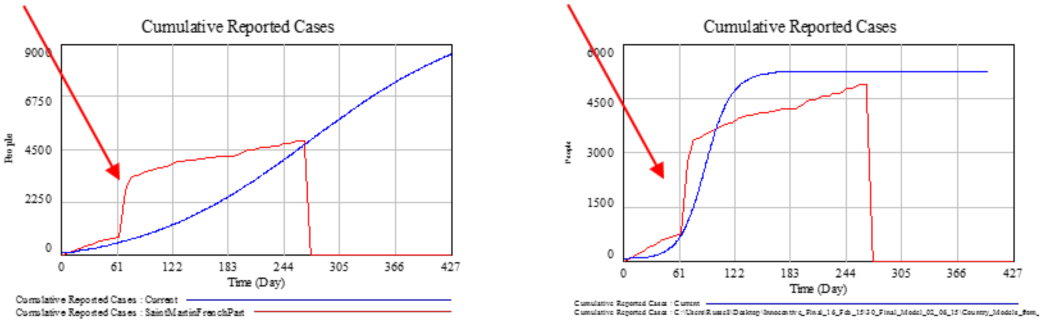
Week	**0**	**2**	**4**	**6**	**8**	**10**	**12**	**14**	**16**	**18**	**20**	**22**	**24**	**26**	**28**	**30**	**32**
Actual	8	127	364	844	1058	6738	10547	14784	19145	23335	28185	33535	36515	36515	50455	54075	57435
Model	8	10	16	30	60	125	268	578	1250	2678	5607	11201	20568	33294	46505	57017	63872
Delta	0	-117	-348	-814	-998	-6613	-10279	-14206	-17895	-20657	-22578	-22334	-15947	-3221	-3950	2942	6437

Table 3: Model Data Comparison for Martinique through Week 32

Table 3 presents a bi-weekly summary of the actual reported cases of CHIKV in Martinique and the output of the model along with a delta between the two. Unlike St. Martin, the actual reported cases did not experience the strong growth in the first 10 weeks of the epidemic. However, the simulation does lag behind the actual data for the first 28 weeks of the time horizon. The two sets of data are slightly correlated with each other, as the coefficient of correlation is 0.61 for Martinique. Like St. Martin, the model generates similar behavior to the actual spread of the CHIKV virus in Martinique. The fact that the model can generate similar behavior to the spread of the virus in multiple countries adds to the validity of the model for use in policy analysis.

Potential Policy Alternatives

In developing potential policy alternatives, and in validating our current model, we have identified several shortcomings in explicitly modeling CHIKV spread. For example, for many of the 58 countries we modeled we had to adjust the *Initial Human Infected Population* to capture the drastic, steep initial exponential increase in cumulative CHIKV cases at the beginning of an outbreak. This is attributable to a lack in the reporting of CHIKV infections initially, as we surmise that only a small percentage of people will report or be diagnosed with CHIKV during the initial part of an outbreak and true reporting doesn't start until the outbreak is already well established. This led to an adjustment in our model. Using St. Martins as a comparison, Figure 11 shows the effect of adding a variable to the model, the *Probability of Reporting*, which better accounts for the sharp growth upon the onset shortly after reported infections.


Current model does not account for sharp initial growth, likely attributable to a delay in reporting cases until the outbreak is known.

The addition of a variable to capture reporting lag, Probability of Reporting (10%) contributes to improved fit here.

Figure 11: Adding the *Probability of Reporting*

This just represents one of the enhancements we can continue to make to the model to better inform policy decisions. Along these lines, additional enhancement of variable representation or additional model structure can capture various potential surveillance and reporting programs considered for implementation.

Other areas of policy analysis to investigate are the effect of vector control efforts and the effect of personal protective measures. The variables identified as having the greatest effect on model behavior and the resultant effect in increasing or decreasing the S-shaped behavior include *Average Mosquito Contact Per Person, Fractional Mosquito Egg Death Rate, Average Mosquito Feedings Per Day*, and *Infectivity* (to a lesser degree). When these variables are increased, the number of CHIKV cases gets large rather quickly. In particular, there is an inability to appropriately balance the sharp exponential growth of reported cases before it quickly explodes . Enhancing our current model with vector control or containment and personal protective measures that balance these variables should be more explicitly included in the structure of the model, balancing the exponential growth aspect associated with spread. Vector control structure can be added explicitly within the mosquito population model, and personal protective measure structure can be implemented to reduce the exposed human population. Variations of these structures can serve to model various policies.

Conclusions and Future Work

The strength of system dynamic modeling lies in its ability to investigate multiple policies or alternatives to a system. The current model is relatively simple, can be run on any computer and the software being used is readily available online to be downloaded to any typical desktop or laptop computer. The current model runs instantaneously. Although this CHIKV model is relatively simple in its current state, it can continue to be enhanced and improved to get better grounded in available data to achieve better forecasting results. Various policies to mitigate the spread of CHIKV can be investigated by changing parameters or modifying the existing model structure, running the new simulation, and analyzing and comparing the resulting output. As an example, specific vector control efforts, and their resultant effects can be analyzed and compared to identify cost effective vector control efforts to best mitigate CHIKV spread. Additionally, this system dynamic model is easily tailored to other epidemiological problems, such as Dengue Fever or even Ebola.

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